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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,884	03/12/2004	Viswanathan Srinivasan	P24615	4898

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
07/08/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/798,884	SRINIVASAN ET AL.
	Examiner	Art Unit
	ARADHANA SASAN	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *117-200* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *117-200* is/are rejected.

7)☒ Claim(s) *191* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Restriction Response

1. Applicant's election of "Bi-layered Tablet" in the reply filed on May 16, 2011 is acknowledged. Applicant notes that a bi-layered tablet is merely a specific form of a dosage form and a tablet. Applicant states that currently all of claims 117-200 read on the elected species. Because applicant did not distinctly and specifically point out the supposed errors in the election of species requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The election of species requirement is therefore made FINAL.

Finality of restriction requirement approved. /Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615

2. Claims 117-200 are included in the prosecution.

Claim Objections

3. Claim 191 is objected to under 37 CFR 1.75(c) as being in improper form because it is dependent on itself. Please see MPEP § 608.01(n). For examination purposes claim 191 was considered as being dependent on claim 190. Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 117-119, 134-139, 166, 167, and 175-179 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara et al. (US 6,699,502).

The claimed invention is a pharmaceutical dosage form which comprises (a) a first drug which comprises at least one morphine derivative having antitussive activity and (b) at least one second drug, wherein a plasma half-life of the at least one second drug differs from a plasma half-life of the first drug and wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70% of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.

Fanara teaches a pharmaceutical composition (including a multi-layered pharmaceutical composition) for oral administration that allows the release of at least one active substance and includes a matrix (Abstract). Fanara teaches: "The release of active substances during oral administration can be controlled by means of matrix-type pharmaceutical compositions" (Col. 1, lines 14-16). The compositions "can be administered in a few daily doses, ideally in a single daily dose" (Col. 1, lines 9-13). Fanara further teaches that: "… it is increasingly advantageous to be able to simultaneously administer by oral route an active substance released immediately after administration, and the same or a second active substance released gradually and regularly after administration … this makes it possible to obtain combined therapeutic effects by means of two active substances having very different pharmacokinetic profiles" (Col. 2, lines 36-50).

Since the same or a second active substance are disclosed in the pharmaceutical compositions (Col. 2, lines 36-50), it is obvious that the therapeutic effect from the controlled release of the actives would be the result of the administration of the pharmaceutical composition.

A person of ordinary skill in the art can interpret the 70% coextensive therapeutic range of the at least second drug as being 70% **within** the therapeutic range of the first drug or that there is 70% **overlap** between the therapeutic ranges of the first drug and the at least second drug.

This reference also teaches that the "controlled-release pharmaceutical compositions can be used in combination with an immediate-release pharmaceutical composition for the same or for another active substance, in a single unit intended to be administered orally" (Col. 3, lines 32-37). This renders obvious the simultaneous or coextensive therapeutic range of more than one active drug in a single dosage form, as instantly claimed.

Fanara teaches that antihistamines, antitussives, such as codeine, morphine, and their pharmaceutically acceptable salts, along with pseudoephedrine, and phenylepherine may be included in the composition (Col. 4, lines 54-67). The pharmaceutical composition can be in the form of tablets (Col. 5, lines 18-20). The tablets can be bilayered (Col. 5, lines 48-58) or multilayered (Col. 6, lines 20-26). Example 7 of this reference discloses a double-layer tablet (with the two layers stuck to each other) containing 15mg doses of hydrocodone bitartrate (10mg of the hydrocodone is in a controlled release layer and 5mg of the hydrocodone is in an immediate release layer (Col. 12, line 25-64).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the pharmaceutical composition having combined therapeutic effects of more than one active substance, as suggested by Fanara, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the pharmaceutical composition as taught by Fanara allows the release of the "active substances such that a satisfactory therapeutic effect is observed over fairly long periods, for example in only one or even two daily doses" (Col. 3, lines 22-27).

The pharmaceutical dosage form comprising a first drug (morphine derivative having antitussive activity) and a second drug where the dosage form provides a plasma concentration within a therapeutic range of the second drug over a period which is coextensive with at least about 70% of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug would have been obvious to one of ordinary skill in the art over Fanara. As mentioned above, Fanara teaches simultaneously administering more than one active substance and combining the therapeutic effects of active substances with different pharmacokinetic profiles (Col. 2, lines 36-50) and includes antitussives, antihistamines, codeine, and morphine as possible active substances in the composition. In order to have the combined therapeutic effects of active substances, it would have been obvious to one with ordinary skill in the art that the period of therapeutic effectiveness of the first active substance would be coextensive with the period of therapeutic effectiveness of the

second active substance, especially if the two active substances are related to similar (antitussive) therapeutic activities.

The elected species of a bilayered tablet would have been obvious to a person with ordinary skill in the art over the Fanara teaching of bilayered tablets and matrix.

6. Claims 120-123, 128-133, 140-153, 155-157, 159-165, 168-174, 180-195, and 198-200 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara et al. (US 6,699,502) in view of Jaeger (US 3,914,425).

The teaching of Fanara is stated above.

Fanara does not expressly teach codeine phosphate as the active substance.

Jaeger teaches an antitussive codeine composition. Example 2 of this reference illustrates a three-layer "pill" or tablet containing codeine phosphate (Col. 2, lines 43-47). "An intermediate layer containing 6mg each of the two active ingredients was protected by a thin coating … and the outer layer contained 18mg codeine phosphate". Jaeger also teaches "preparations containing codeine may additionally contain antihistamines such as triprolidine hydrochloride, decongestants such as pseudoephedrine hydrochloride, and expectorants such as glyceryl guaiacolate" (Col. 3, lines 3-7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the pharmaceutical composition having combined therapeutic effects of more than one active substance, as suggested by Fanara, in view

of the codeine phosphate and second active substances (antihistamines, decongestants, and expectorants) as suggested by Jaeger and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the pharmaceutical composition as taught by Fanara allows the release of the "active substances such that a satisfactory therapeutic effect is observed over fairly long periods, for example in only one or even two daily doses" (Col. 3, lines 22-27). The second drugs taught by Jaeger would have been obvious to one of ordinary in the art as supplementing the antitussive first drugs for ameliorating cough symptoms.

Regarding instant claims 128-130, one with ordinary skill in the art would use the teachings of Fanara and Jaeger to make a pharmaceutical composition by using drug combinations (antitussives, antihistamines, decongestants, expectorants) with drugs having different plasma half-lives in order to optimize the release of drugs over time. Drugs that are part of the immediate release would have a different plasma half-life than drugs that are part of the controlled release in order to maintain drug release for optimal therapeutic effect.

Regarding instant claims 131-133,145-146, 159, and 161, one with ordinary skill in the art would use the teachings of Fanara and Jaeger to make pharmaceutical compositions using drugs with different pharmacokinetic profiles (Fanara, Col. 2, lines 46-50). The claim limitations of periods of plasma concentration within the therapeutic range of the second drug being coextensive with at least about 80%, 90% or 95% of periods of plasma concentration within the therapeutic range of the first drug would

have been obvious over the different pharmacokinetic profiles taught by Fanara in view of the antitussive codeine composition taught by Jaeger.

7. Claims 124-127, 154, 158, and 196-197 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara et al. (US 6,699,502) in view of Jaeger (US 3,914,425) and further in view of Findlay et al. (US 4,650,807).

The teachings of Fanara and Jaeger are stated above.

Fanara and Jaeger do not expressly teach chlorpheniramine, promethazine, and guaifenesin.

Findlay teaches antihistaminic compositions. These compositions include tablets (Col. 5, lines 33-35). Antihistamines such as pheniramines, and promethazine are disclosed (Col. 1, lines 26-28). It is also taught that, "the active compound may be formulated with a sympathomimetic agent such as decongestants pseudoephedrine or phenylpropanolamine, an antitussive such as codeine … or an expectorant such as guaifenesin" (Col. 5, lines 9-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the pharmaceutical composition with combined therapeutic effects of more than one active substance, as suggested by Fanara, in view of the codeine phosphate and second active substances (antihistamines, decongestants, and expectorants) as suggested by Jaeger and further in view of the specific antihistamines and expectorant as suggested by Findlay and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the specific active substances taught by Findlay supplement the antitussive first drugs for ameliorating cough symptoms.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 117-200 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 75-100, and 104-146 of copending Application No. 10/736,902 ('902 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because the first drug of the instant application is a morphine derivative, whereas the first drug of '902 is promethazine and a pharmaceutically acceptable salt thereof. One with ordinary skill in the art would use various drugs that were compatible in the

composition. Promethazine is an antihistamine and since an antihistamine can be a component of the instant dosage form (second drug of instant claim 121), one with ordinary skill in the art would be motivated to use it in the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 117-200 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-87 of copending Application No. 10/939,351 ('351 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because the first drug of the instant application is a morphine derivative, whereas the first drug of '351 is phenylepherine and a pharmaceutically acceptable salt thereof. One with ordinary skill in the art would use various drugs that were compatible in the composition. Phenylepherine is a decongestant and since a decongestant can be a component of the instant dosage form (second drug of instant claim 5), one with ordinary skill in the art would be motivated to use it in the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 1-52, 72-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 10-20, 25, 27-39, 68-76, and 80-81, and 84 of copending Application No. 11/012,267 ('267 hereinafter). Although the conflicting claims are not identical, they are not patentably

distinct from each other because the first drug of the instant application is a morphine derivative, whereas the first drug of '267 is diphenhydramine and a pharmaceutically acceptable salt thereof. One with ordinary skill in the art would use various drugs that were compatible in the composition. Diphenhydramine is an antihistamine and since an antihistamine can be a component of the instant dosage form (second drug of instant claim 5), one with ordinary skill in the art would be motivated to use it in the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 117-200 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-48, and 56-62 of copending Application No. 11/115,293 ('293 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because the first drug of the instant application is a morphine derivative, whereas the first drug of '293 is promethazine and a pharmaceutically acceptable salt thereof. One with ordinary skill in the art would use various drugs that were compatible in the composition. Promethazine is an antihistamine and since an antihistamine can be a component of the instant dosage form (second drug of instant claim 5), one with ordinary skill in the art would be motivated to use it in the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 117-200 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6-8, 12-13, 17-20, 21-24, 28-34, 38-41, 47-50, 60-65, 67-70, 73-74, 79-83, 86-90, 92, 95-96, 114, 117-119 of copending Application No. 11/115,321 ('321 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because the first drug of the instant application is a morphine derivative, whereas the first drug of '321 is an antitussive that comprises a morphine derivative. Since a morphine derivative having antitussive activity is a component of the instant dosage form (first drug of instant claim 1), one with ordinary skill in the art would be motivated to use it in the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615